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## **Extension of computer aided solvent selection and design framework – organic solvents for phase transfer catalysis**

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Nowadays solvents are used in many industrial sectors such as, chemical, pharmaceutical, food, and agrochemical industries within a wide range of applications including extraction and cleaning, separation processes, organic synthesis, and product delivery. Therefore, solvent selection represents a complex problem for solvents must satisfy cost, processing, environmental, safety and health related specifications.

Computer-aided molecular design techniques are being increasingly used to identify promising candidates from an enormous range of potential alternatives. The aim of such techniques are to develop molecules directly according to property and performance specifications and to combine various sets of structural groups (building blocks) to form chemically feasible molecules in systematic way.

The objective of this work is to present a systematic framework [1] and its software implementation for selection and design of solvents for most of the common solvent applications, including organic synthesis, complex reactive systems, solvent-based separations and phase-transfer catalysis (PTC) reactions. The framework is a combination of computer aided tools and methods and knowledge from industrial practice. The framework is divided into modules for solvent selection and design for organic synthesis, separation processes, phase-transfer catalysis, cleaning and formulated products. In this paper, the first three modules will be highlighted through appropriate case studies.

The first module is dedicated to solvent selection and design for organic synthesis. This module is based on solvent selection methodology for organic synthesis [2] and handles single and multi-step chemical synthesis problems as well as solvent substitution feature. Case study for multi-step organic reaction is presented.

The second module of the framework combines a model-based method for solvent screening and solvent mixtures design for pharmaceutical applications. The solvent screening method is based on the theory of the conceptual segments (hydrophobic, polar and hydrophilic), the so-called NRTL-SAC model. A group contribution model for prediction of the conceptual segments has been used in order to make the method completely independent from the availability of experimental data. The extended method (to be called UNISAC) allows the description and characterization of the API molecule so that making possible the evaluation of its solubility in different solvents. Case study for solvent mixture design is presented.

The third module is solvent selection in phase-transfer-catalysis. This module makes use of a model-based strategy for selection of the best organic solvent in PTC-based reacting

systems where the organic solvent plays an important role since solubility of different forms of the PTC in the organic solvents affects ultimately the catalyst partition coefficients. Through this module, it is possible to find opportunities for improving reacting system performance and replacement of solvents. A case study showing improvements of the reaction operation is presented.

### **References:**

- [1] Gani R., Mitrofanov I., Conte E., Abildskov J., Sin G. Computer Aided Solvent Selection and Design Framework. AIChE-2011
- [2] Folic, M., Gani, R., Jiménez-González, C., Constable, D.J.C., 2008. Systematic Selection of Green Solvents for Organic Reaction Systems. Chinese Journal of Chemical Engineering. 16(3), 376-383.